Appln No.: 09/996,128
Amendment Dated: February 3, 2005
Reply to Office Action of November 3, 2004

REMARKS/ARGUMENTS

This is in response to the Office Action mailed November 3, 2004 for the above-captioned application. Reconsideration and further examination are respectfully requested.

Applicants note that the Examiner has not acknowledged consideration of the Information Disclosure Statement filed on March 5, 2002. This Information Disclosure Statement appears in the electronic file wrapper available to Applicants on-line, so it assumed that the Examiner has access to it as well. Consideration and return of an initialed copy of the PTO 1449 are requested.

The specification has been amended to reflect the patent number of the granted parent case and the filing date of the PCT application in accordance with the Examiner's remarks.

Claims 1, 2, 4, 5, 10-12, 17 and 19-24 were examined in this application.

The Examiner rejected claims 1, 2, 4, 5, 10, 11, and 19-23 under 35 USC § 112, first paragraph for failing to comply with the written description requirement. The Examiner states that the written description in the present application only sets forth the sequence of human tyrosinase found in Seq. ID. No. 1, and therefore that the scope of written description is limited to human tyrosinase (as set forth in claim 12) and the Seq. ID No. 1 (as set forth in claim 24). Applicants submit that this argument is both factually and legally erroneous.

Looking first at the factual basis for the rejection, the Application includes the sequence for murine tyrosinase (Seq. ID No. 2). It also shows experiments using gp75 as the differentiation antigen, and discloses other differentiation antigens associated with melanoma on Page 1, lines 9-11. Thus, the basis for the Examiner's statement that there is only written description for human tyrosinase is not clear.

Furthermore, the issue of compliance with the written description requirement should be focused on the invention. The cases the Examiner cites, however, deal with the amount of description required when the invention is a protein or nucleic acid *per se*. That is not the case here, where the sequences of the numerous differentiation antigens are known in the art. Thus the statement by the Examiner that "with the exception of Sequnce ID No: 1 and 2 from humans (actually sequence ID No: 2 is murine, not human) the skilled artisan cannot envisage the plethora of differentiations antigens, and with particularity tyrosinase" is in error. Further, there is no question concerning the isolation procedures since this has already been done by others. The skilled artisan would only need to look to the myriad resources, including the Entrez Pub Med collection, and the published literature as whole to not only envisage the sequence but to know what it is. As stated in Written Description guidelines, MPEP § 2163, II, A, (3), the description need only describe in detail that which is new or not conventional. *See Hybritech v.*

Monoclonal Antibodies, 802 F.2d at 1384, 231 USPQ at 94." The rejection in this case disregard this statement of the law. There can be no doubt that Applicants invented what is now **claimed**, that is a method of using xenogeneic sequences, known in the art to be melanoma-associated differentiation antigens,[1] as a treatment for melanoma. Thus, the rejection under 35 USC § 112, first paragraph, should be withdrawn.

Th Examiner also rejected claims 1, 2, 4, 5, 10-12 and 19-23 as obvious over Disis et al, in view of Natzger et al. As a first matter, Applicants submit that the Examiner must consider the effective filing date as to each claim since the priority application 60/032,535 was filed before or on the same day as Natzger was published. (See Exhibit A) Accordingly, as to any claim receiving the benefit of this filing date, Naftger is not a reference, and the rejection should be withdrawn. Since no image is available in the PAIR system for this provisional application, a highlighted copy is attached for the Examiner's convenience. (Exhibit B)

Claim 1 of the present application recites a method of treating melanoma in a mammalian subject by administering a xenogeneic differentiation antigen expressed by melanoma cells. The '535 provisional states on Page 1, third paragraph, that

> A second aspect of the invention is a method of inducing immunity to a tumor in a subject comprising the step of immunizing the subject with a differentiation antigen specific to the type of tumor which has been expressed in a host of a different species from the subject. A specific, non limiting example of this aspect of the invention is the use of mouse gp75 to induce a protective effective (sic) against melanoma in humans.

The provisional continues on page 2, second paragraph with a listing of melanocyte differentiation antigens that include tyrosinase, gp75, gp100/pMel and MART-1. Further, the paragraph bridging Pages 9 and 10 discloses experimental results in which human gp75 is shown to induce autoantibodies against murine gp75 when adminitered to mice. Thus, this is a specific example and reduction to practic of the generic subject matter of claim 1. This disclosure also provides specific support for claim 4, in which the xenogeniec antigen is identified as human and the subject is a non-human mammal (i.e, a mouse), claim 7 wherein the xenogeneic antigen is a murine antigen, and claim 8, wherein the subject is human. Thus, the art rejection as applied to claims 1, 4, 7 and 8 should be withdrawn.

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[1] That the present disclosure is based on those antigens currently known to be associated with melanoma does not exclude from the coverage of the claims the use of some later discovered differentiation antigen in the method of the present invention.

Turning now to the merits of the rejection, the Examiner asserts that the combination of Disis and Naftzger render the claimed invention as set forth in claim 1, 2, 4, 5, 10-12, and 19-23 obvious. Applicants respectfully disagree. As a first matter, with respect to claims 2, 4, 5, 12, 21 and 22, there is no teaching in the reference concerning tyrosinase as required in these claims. The Examiner does not offer a reference teaching tyrosinase and alleged to provide a suggestion of the ability to use tyrosinase in place of gp75. Instead, the Examiner says that this substitution is oibvious because"gp 75 is closely related to tyrosinase." This is in direct contradiction to the statements made by the Examiner in connection with the restriction requirement which has been maintained and made final, in which the Examiner expressly states that "the differentiation antigens [including gp75 and tyrosinase] are patentably distinct and structurally different from one another and would elicit different immune response." (Office Action, Page 2.) Accordingly, Applicants submit that the rejection should be withdrawn.

It is noted that the Naftzger paper does disclose tyrosinase in Column 1 on page 14809. This disclosure is coextensive with the disclosure in the original provisional application, and therefore the claims relating to tyrosinase should either be deemed supported by the provisional application, such that Naftzger is not a reference, or Natzger should be insufficient to establish a reasonable expectation of success with respect to tyrosinase and other melanoma-associated antigens.

It is further noted that the Examiner has not addressed the limitation of claims 10-12 concerning the use of a vector encoding the differentiation antigen as the therapeutic agent. Both Disis and Natzger teach immunization with peptides/proteins, not nucleic acids. The Examiner has not indicated why immunization with the nucleic acid would have been suggested by the art, or provided a reasonable expectation of success.

The Examiner has also not addressed the additional limitation in claim 19 concerning of a xenogeneic antigen followed by or co-administered with a syngeneic antigen. The Natzger reference makes it clear that syngeneic gp75 does not induce an immune response (See Page 14810, Col. 2, first full paragraph). Thus, absent some argument as to why the invention as set forth in claim 19 would have been obvious, the rejection should be withdrawn.

Finally, with respect to claims 20-23, the Examiner has not addressed the treatment of the specific condition, canine malignant melanoma, nor apparently considered the results reported. Canine malignant melanoma is a highly aggressive metastatic neoplasm and is resistant to chemotherapy. (Specification, Example 8). The references do not suggest the success obtained against this specific disease with this treatment, which achieved extended survival for period in the neighborhood of a year for a significant portion of the dogs treated. Thus, the rejection of claims 20-23 should be withdrawn.

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The Examiner also provisionally rejected claims 1, 2, 4, 5, 10-12, 17 and 19-24 for obviousness-type double patenting in view of co-pending application 10/041,410. Applicants will address this rejection through filling of a terminal disclaimer if appropriate when claims are found to be allowable in this application or in the cited application. It is noted, however, that as to claims 17 and 24, which are not rejected under either § 112 or § 103, the Examiner has not addressed why the specific limitations of these claims, which specify the use of Seq. ID No.1 would be deemed to be obvious over the more generic claims of the '410 application. Such an analysis is necessary to support a double-patenting rejection of these claims.

For these reasons, this application is now considered to be in condition for allowance and such action is earnestly solicited.

Respectfully submitted,

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